REMARKS

Claims 1 and 4-13 are all the claims pending in the application. Claim 1 is amended. Support is found, for example in the original claims and the working examples of the specification. No new matter is presented.

Applicant would like to remind the Examiner that a Petition to Make Special was filed and accepted in this case and therefore, the examination of the application is to be expedited.

I. Response to Claim Objections

Claims 1 and 4-13 are objected to because the term "pirfenidone" after "5-methyl-1-phenyl-2-(1 H)-pyridone" is considered to be needlessly duplicative.

Claim 1 is amended herein by deleting the term "Pirfenidone", thereby obviating the objection to the claim.

Accordingly, Applicant respectfully requests withdrawal of the objection.

II. Response to Claim Rejection under 35 U.S.C. § 103 -Obviousness

Claims 1 and 4-13 are rejected under 35 U.S.C. §103(a) as being unpatentable over Scheiwe et al (US 6,492,395) in view of Iyer et al (US 2004/0033257). The Examiner also did not find the Amendment and Declaration evidence filed July 28, 2008 to be persuasive.

1. First, the Examiner states that there is no recitation that the compositions have to be stable at lower temperatures.

Applicant traverses this aspect of the rejection and submits that the evidence presented establishes that the composition of the present invention possesses non-obvious properties which are not possessed by the compositions of the prior art. There is no requirement that these

properties have to be recited in the claims. See, e.g., *In re Chu*, 66 F.3rd 292, 299 (Fed. Cir. 1995) where the court found that there are no cases supporting the position that a patent applicant's evidence and/or arguments traversing a § 103 rejection must be contained within the specification. Unexpected results need to be commensurate in scope with the claims, which means that the unexpected results must be due to the claimed features and not to unclaimed features. Thus, properties/effects of an invention are a result of the claimed features and need not be recited. The data presented is evidence in support of the patentability of the claimed invention, which refutes the Examiner's position. The present claims recite a composition which is different from the prior art and it is the difference in the composition that contributes to the unexpectedly superior results of the claimed invention. Id. Therefore, the claims recite the elements which distinguish the claimed invention and which contribute to the unexpectedly superior results obtained as supported by the Declaration evidence submitted.

2. The Examiner's second point is that the claims use the term "capable" with respect to the solvent being able to dissolve the pirfenidone compound which, according to the Examiner, means that the solvent is capable of performing the function, it does not mean that the composition has to comprise 10% to 25% pirfenidone.

Claim 1 is amended to recite that the composition comprises 5-methyl-1-phenyl-2-(1 H)-pyridone in a concentration of 10-25%, thereby obviating this aspect of the rejection.

3. The Examiner also maintains that Scheiwe discloses a solution because the compound is dissolved in a solvent and that Scheiwe also shows the solvent is capable of dissolving pirfenidone at 10% even though this was not the final composition. In response to the arguments presented in the Response filed July 28, 2008, the Examiner asserts that, in this

instance, a market pressure exists in the medical/pharmaceutical industries to stabilize solutions comprising pirfenidone and it would have been obvious to have searched for a stronger solubilizer to ensure the pirfenidone stayed in solution.

The Examiner further asserts that the secondary reference, Iyer, discloses solvents that dissolve a water insoluble compound, which include propylene glycol as well as diethylene glycol monoethyl ether (DGME). The Examiner therefore concludes that since pirfenidone is slightly soluble, it would have been reasonable to conclude that solvents that dissolve an insoluble substance would dissolve a slightly soluble substance. The Examiner further states that Iyer also discloses DGME as a powerful solubilizer and that DGME is equivalent to polyethylene glycol (paragraph 0014), which is a plasticizer in the primary reference and disclosed as an equivalent to polypropylene glycol. Thus, the Examiner takes the position that it is reasonable to conclude that since polypropylene glycol dissolves pirfenidone, then DGME will also dissolve pirfenidone. In regard to the argument that the compositions in Iyer are capsules, the Examiner states that loratadine is dissolved before being encapsulated therefore it is in a solution.

Applicant submits that the Examiner's position is based on improper hindsight reasoning and is legally improper.

First, Scheiwe does not disclose a solution of pirfenidone in DGME as a solvent as required by the claims. The claims require pirfenidone in a concentration of 10-25% and DGME as a solvent. Scheiwe does not disclose, teach or suggest this specific composition. As Applicant has previously pointed out Scheiwe teaches away from compositions comprising pirfenidone in an amount of 10% with standard excipients in teaching that the preferred

concentration of pirfenidone is 3 to 7% and in teaching a comparative example wherein pirfenidone is employed in an amount of 10% wt/wt and found to be unsuitable. Specifically, Scheiwe et al teaches that standard excipient preparations are unsuitable for use in the preparation of pharmaceutically acceptable topical formulations such as ointments containing a sufficient dosage of the active ingredient because pirfenidone tends to physically destabilize emulsions and other colloidal systems. Column 1, lines 59-67. Scheiwe et al further teaches that the ointment preparations of Comparative Example 1 developed phase separation effects, the emulsion became inhomogeneous by coalescence effects and also large crystals developed upon storage. Thus, based on the teachings of Scheiwe et al taken as a whole, one of ordinary skill in the art would not have expected to achieve a suitable stable liquid formulation comprising 10 to 25% pirfenidone and Scheiwe does not teach or suggest DGME as a solvent for concentrations of 10 to 25 % pirfenidone.

Instead Scheiwe teaches specific formulations employing 3-7 wt% of pirfenidone (see column 3) and compositions characterized in that the excipient comprises one or more plasticizers, one or more antioxidants, one or more gel-forming agents, and sufficient pH adjusting agent, see column 2, lines 10-30. However, there is no teaching or suggestion of modifying, substituting or adjusting the plasticizer specifically of all of the ingredients said to be characteristic of the excipient. It is only with improper hindsight that the Examiner has chosen the plasticizer of Scheiwe as the ingredient to be modified, substituted or adjusted as taught by Applicant's specification. It is only with the advantage and knowledge of Applicant's specification that the Examiner could have arrived at this conclusion since the use of DGME as the solvent for pirfenidone is the solution to the problem with which Applicant was faced at the time of the invention. Defining the problem with which Applicant was faced in terms of the

solution is improper hindsight in the selection of the prior art applied by using the invention as an editing standard of the most applicable references. *See, Monarch Knitting Machinery Corporation, et al v. Sulzer Moratt, et al.*, 139 F.3d 877 (Fed. Cir. 1998).

4. Regarding the Declaration, the Examiner states although the compositions in DGME were more stable, the claims read on a solution at any temperature and the DGME is at any concentration, which encompasses amounts other than that in the disclosed Declaration. The Examiner further asserts that there also is no limitation in the claims that the compositions have to be stable at temperatures other than room temperature. Additionally, the Examiner points out that Applicant uses more DGME in the compositions of the instant claims than propylene glycol in the compositions representing the compositions of the prior art. The Examiner asserts that Applicant has not shown how stability is affected at 65% of propylene glycol as disclosed in the reference or at 75% as in the example of the instant invention. Furthermore the Examiner states that the examples of the prior art uses polypropylene glycol, not propylene glycol. Therefore it cannot be determined if the compositions yield unexpected results. Finally, the Examiner states that Applicant recites "a solvent capable of dissolving said 5-methyl-1-phenyl-2-(1 H)-pyridine". The term "capable" indicates that the compositions do not have to have 10 to 25% pirfenidone, only that the solvent is "capable of" dissolving 10 to 25% pirfenidone.

As stated above, there is no requirement that the claims recite unexpected properties of the claimed invention. See also *In re Chu* cited above.

With respect to the Examiner's position regarding the amount of DGME, Applicant notes that claims 9-11 recite specific amounts of DGME. Claim 1 is amended herein to recite a

concentration range of DGME based on the disclosure in the specification, e.g., 70-80 % by weight as in the working examples of the specification.

In regard to the Examiner's comments that Scheiwe employs the use of "polypropylene glycol" in its formulations, Applicant notes that the USP and other pharmacopoeias include standards for "propylene glycol", which is "mono-propylene glycol". Applicant submits that the "polypropylene glycol" is not currently recognized or specified in any pharmacopoeia monograph. On the other hand, propylene glycol has an official USP monograph. Therefore, the comparison made in the Declaration provided by Dr. Seth employing propylene glycol is closer to the present invention. See MPEP 716.02(e)(I).

As to the amount of propylene glycol used in the examples of Scheiwe as compared to the amount of DGME used in the inventive examples of the present invention in the Declaration, Applicant submits that one of ordinary skill in the art would recognize that an increased amount of propylene glycol would be expected to have more adverse results than the comparative example in the Declaration, which employs 50/50 propylene glycol/water, because the use of propylene glycol itself in concentrations of more than 20-30% for dermal applications, is not practical due to its adverse effects of dehydrating the skin and is therefore undesirable for use in a formulation for avoiding skin irritation or mucous membranes as in the present invention. See, e.g., the paragraph bridging pages 2-3 of the specification.

With regard to the Examiner's statement that Applicant has not shown how stability is affected at 65% propylene glycol or at 75% as in the example of the present invention, Applicant submits that Applicant is not required to compare the claimed invention to that which does not exist in the prior art. See MPEP 716.02(e)(III). In this case Scheiwe teaches that the plasticizer

is employed in an amount of 5 to 65 wt.% (see column 3), but Scheiewe does not specifically teach the use of propylene glycol in an amount of 65 wt% and there is no specific embodiment employing propylene glycol in an amount of 65 wt%. Further, the Examples of Scheiwe employ polypropylene glycol. Thus, there is no requirement for Applicant to compare the claimed invention with a comparative example employing 65 % or 75% of propylene glycol as the prior art does not teach such an embodiment.

The Examiner further suggests that Applicant distinguishes the compositions from those that use DGME as the primary solvent and those that have a miniscule amount of DGME, which is used to dissolve the pirfenidone that is not dissolved in water.

Claim 1 is amended to recite a concentration range of DGME of 70-80% as supported by the original claims and working examples of the specification, thereby obviating this aspect of the rejection.

The Examiner states that Iyer et al is relied upon for the disclosure of solvents that dissolve poorly soluble compounds. However, there is no reason to combine Scheiwe et al and Iyer et al.

Iyer et al does not disclose, teach or suggest a liquid composition comprising pirfenidone, much less 10 to 25% pirfenidone and DGME and Iyer et al does not recognize the problems associated with making pirfenidone formulations at higher concentrations. Iyer et al teaches gelatin capsules comprising loratidine. Iyer et al specifically describes a formulation of loratidine, solubilized in a mixture of solvent and emulsifiers and which is specifically to be used in making soft gelatin capsules of this particular drug. The maximum concentration of the drug (as shown in Table 1 at paragraph [0030]) reached in the solvent mixture is 8% drug. Transcutol

P alone is only one component along with a mixture of other components of the formulation (for making soft gelatin capsules of loratidine). Iyer et al teaches a different dosage form of a different drug in a lower concentration and is not a true solution, but a suspension in a solvent system, which is not at all relevant to the present invention. Further, Iyer et al can not be applied to all kinds of drug molecules, which are poorly water soluble. Thus, one of ordinary skill in the art would not have been motivated to modify the working examples of Scheiwe et al based on the teachings of Iyer et al with a reasonable expectation of success in achieving a liquid composition comprising pirfenidone in a concentration of 10 to 25% as in the present claims. Hence, Iyer et al does not teach or suggest the presently claimed invention and does not remedy the deficiencies of Scheiwe et al.

Additionally, there is no apparent reason to combine Scheiwe et al and Iyer et al. Specifically, Scheiwe et al teaches topical compositions comprising pyridone derivatives, more specifically pirfenidone, whereas Iyer et al teaches gelatin capsules comprising loratidine. Loratidine is not a pyridone derivative and Applicant has pointed out that there are significant structural differences between loratidine and pirfenidone, such that one of ordinary skill in the art would not consider the compounds to possess similar solubility and stability characteristics. Therefore, there is no apparent reason for one of ordinary skill in the art to expect a solvent suitable for loratidine to be suitable for pirfenidone.

The Examiner admits that Iyer et al does not specifically disclose pirfenidone as a drug that could be dissolved in the solvents described therein, but the Examiner asserts that Iyer discloses solvents that dissolve a water soluble compound and these solvents include propylene glycol as well as diethylene glycol mono ethyl ether (DGME). However, Applicant submits that

the Examiner's conclusion is improperly based on hindsight reasoning. Considering the differences between the formulations (i.e., topical formulations vs. gelatin capsules for oral administration) and active ingredients (i.e., pyridone derivatives, such as pirfenidone vs. loratidine) taught by Scheiwe et al and Iyer et al, one of ordinary skill in the art would not have been motivated to combine the references as suggested by the Examiner.

Iyer et al does not teach that Transcutol P (or any other solvents mentioned) is a suitable solvent for all poorly soluble drugs and therefore it is not reasonable to assert that based on the teachings of Iyer et al that Transcutol P is a suitable solvent for loratidine, one of ordinary skill in the art would automatically expect Transcutol P to be a suitable solvent for pirfenidone taught by Scheiwe et al simply because pirfenidone is also a poorly soluble drug. The bottom line is that there is no apparent reason to choose DGME as a solvent to be used in combination with pirfenidone or to choose pirfenidone as the poorly water soluble compound in combination with DGME based on the teachings of Scheiwe et al and Iyer et al. It is only with the knowledge of the teachings in Applicant's specification that the Examiner has arrived at a conclusion of obviousness and as such, the Examiner has engaged in improper hindsight reasoning as there is no apparent reason for combining the references.

Accordingly, the present invention is not rendered obvious over the cited references

In view of the above, Applicants respectfully request withdrawal of the §obviousness rejection.

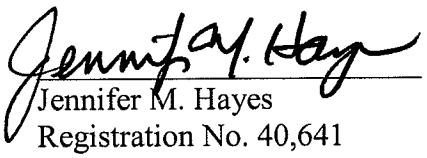
III. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the

Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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